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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,079	12/02/2003	Peng Cho Tang	034536-0904	2712
22428	7590	02/25/2005	EXAMINER	
FOLEY AND LARDNER SUITE 500 3000 K STREET NW WASHINGTON, DC 20007			BALASUBRAMANIAN, VENKATARAMAN	
		ART UNIT	PAPER NUMBER	
			1624	

DATE MAILED: 02/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/725,079	TANG ET AL.	
	Examiner Venkataraman Balasubramanian	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 10 December 2004.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-9, 18 and 38-42 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-9, 18 and 38-42 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                                                        |                                                                             |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | Paper No(s)/Mail Date. _____                                                |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|                                                                                                                        | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

Applicants' response, which included cancellation of claims 10-17, 19-37, addition of new claims 38-42 and amendment to claims 1-9 and 18, filed on 12/10/2004, is made of record.

Claims 1-9, 18 and 38-42 are now pending. In view of applicants' response , the following apply.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 18 and 38-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim and share the same limitation

1. Recitation of "C-amido" in the definition of R<sup>1</sup> in claim 1, renders the claim 1 indefinite as the term "C-amido" is ambiguous. First of all, it is not clear whether the term to treated as an CONH<sub>2</sub> group with the nitrogen unsubstituted or to include N-substituted group. Secondly the C-amido appears to specify link through CO of the amide but it is appended to nitrogen of the indolinone ring. How can such a group be C-amido? Note this group appears at various variable group definition and hence renders claim 1 and other dependent claims indefinite.

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This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included. Applicants' traversal to overcome this rejection is not persuasive. As recited the said substituent appears to be divalent and it is not clear what else is appended. Applicants argue that one trained in the art would know but these are compound claims and hence should be defined precisely.

Hence, this rejection is maintained.

2. Recitation of "sulfonyl" in the definition of R<sup>1</sup> in claim 1, renders the claim indefinite as the "sulfonyl" group is a divalent group and what is appended to the free valence of the group is not defined.

This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included. Applicants' traversal to overcome this rejection is not persuasive. As recited the said substituent appears to be divalent and it is not clear what else is appended. Applicants argue that one trained in the art would know but these are compound claims and hence should be defined precisely.

Hence, this rejection is maintained.

3. Similarly, recitation of "sulfinyl", "sulfonyl" or "sulfonamido" in the definition of R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> in claim 1, renders the claim indefinite as these groups are divalent group and what is appended to the free valence of the group is not defined. See also recitation of "carbonyl" group. What is appended to the free valence of this divalent group also remains unknown.

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This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included. Applicants' traversal to overcome this rejection is not persuasive. As recited the said substituent appears to be divalent and it is not clear what else is appended. Applicants argue that one trained in the art would know but these are compound claims and hence should be defined precisely.

Hence, this rejection is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of protein kinase catalytic activity of the claimed compounds, does not reasonably provide enablement for modulation of protein kinase catalytic activity of the claimed compounds. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry - to use the invention. Any claim not specifically rejected is rejected as being dependent on a rejected claim and share the same limitation.

"The factors to be considered in making an enablement rejection have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability

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or unpredictability of the art and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546.

Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claims 38-42 recite "a method for modulation of catalytic activity of a protein kinase" and specification pages 121-170 discusses several assay protocols which appear to rely on inhibition of kinase. The term "Modulation" encompasses both catalytic activation and inhibition. However, the compounds were not shown to have all these properties. The specification only provides test data related to inhibition. The specification did not provide any competent tests or data to establish that the compounds have the claimed 'protein kinase modulating activity'. Mechanisms underlying the complex regulation of catalytic activity with a single known protein kinase and various other protein kinase generically claimed need further investigation with combined molecular, biochemical and functional approaches. This establishes the uncertainties and the level of unpredictability in the relevant state of the art and

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therefore, one of ordinary skill in the art would be required to go through undue experimentation to find the modulating activity of the compounds.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 6-8 and 38-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,677,368. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-3, 6-8 and 10-37 are also embraced in the claims 1-19 of US 6,677,368. Note when instant J = N, R<sup>1</sup> and R<sup>2</sup> are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-19 of US Patent 6,677,368.

This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included in this rejection.

Applicants' traversal is not persuasive.

First of all, examiner had indicated where the subject matter overlaps. In this case, when instant Q is a pyrrole (J=N, M, K, L are carbon), the compounds , composition ad method of use are obvious over the said claims of US patent 6,677,368.

Contrary to applicants' urging claim 9 is not rejected and partial overlap dose not preclude obviousness type double patenting rejection.

Claims 1-3, 6-8, 18 and 38-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,642.232. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-3, 6-8 and 10-37 are also embraced in the claims 1-25 of US 6,642,232. Note when instant J = N, R<sup>1</sup> and R<sup>2</sup> are hydrogen, Z= carbamido, the subject matter embraced in the instant claims are also embraced in the claims 1-25 of US Patent 6,642,232.

This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included in this rejection.

Applicants' traversal is not persuasive.

First of all, examiner had indicated where the subject matter overlaps. In this case, when instant Q is a pyrrole (J=N, M, K, L are carbon), the compounds , composition ad method of use are obvious over the said claims of US patent 6,642,232.

Contrary to applicants' urging claim 9 is not rejected and partial overlap dose not preclude obviousness type double patenting rejection.

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Claims 1-4, 6-9, 18 and 38-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,635,640. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-4, 6-9 and 18 are also embraced in the claims 1-13 of US 6,635,640. Note when instant Q is same as the second choice of Q in the US 6,635,640, and both R<sup>1</sup> and R<sup>2</sup> are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-13 of US Patent 6,635,640.

This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included in this rejection.

Applicants' traversal is not persuasive.

First of all, examiner had indicated where the subject matter overlaps. In this case, when instant Q is second choice of Q of the said patent, the compounds , composition ad method of use are obvious over the said claims of US patent 6,635,640.

Contrary to applicants' urging, partial overlap dose not preclude obviousness type double patenting rejection.

Claims 1-9, 18 and 38-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,486,185. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-37 are also embraced in the claims 1-40 of

US 6,486,185. Note when instant R<sup>1</sup> and R<sup>2</sup> are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-40 of US Patent 6,486,185.

This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included in this rejection.

Applicants' traversal is not persuasive.

First of all, examiner had indicated where the subject matter overlaps. In this case, when instant Q is same as Q in the said US patent, the compounds , composition ad method of use are obvious over the said claims of US patent 6,486,185.

Contrary to applicants' urging, partial overlap dose not preclude obviousness type double patenting rejection.

Claims 1-3, 6-8 and 10-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,395,734. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-3, 6-8 and 10-37 are also embraced in the claims 1-23 of US 6,395,734. Note when instant J = N, R<sup>1</sup> and R<sup>2</sup> are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-23 of US Patent 6,395,734.

This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included in this rejection.

Applicants' traversal is not persuasive.

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First of all, examiner had indicated where the subject matter overlaps. In this case, when instant Q is a pyrrole, the compounds , composition ad method of use are obvious over the said claims of US patent 6,395,734.

Contrary to applicants' urging, partial overlap dose not preclude obviousness type double patenting rejection.

Claims 1-9, 18 and 38-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 6,316,635. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-37 are also embraced in the claims 1-29 of US 6,316,635. Note when instant M = N and/or J = N, R<sup>1</sup> and R<sup>2</sup> are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-29 of US Patent 6,316,635.

This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included in this rejection.

Applicants' traversal is not persuasive.

First of all, examiner had indicated where the subject matter overlaps. In this case, when instant Q is imidazole (M = N and/or J = N, R<sup>1</sup> and R<sup>2</sup> are hydrogen) the compounds , composition ad method of use are obvious over the said claims of US patent 6,316,635.

Contrary to applicants' urging, partial overlap dose not preclude obviousness type double patenting rejection.

Claims 1-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,313,158. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-37 are also embraced in the claims 1-21 of US 6,313,158. Note when instant J = N or S or O and R<sup>1</sup> and R<sup>2</sup> are hydrogens, the subject matter embraced in the instant claims are also embraced in the claims 1-21 of US Patent 6,313,158.

This rejection is same as made in the previous office action except that cancelled claims are excluded and newly added claims are included in this rejection.

Applicants' traversal is not persuasive.

First of all, examiner had indicated where the subject matter overlaps. In this case, when instant Q is pyrrole or furan or thiophene (J = N or S or O and R<sup>1</sup> and R<sup>2</sup> are hydrogen) the compounds , composition ad method of use are obvious over the said claims of US patent 6,6313,158.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (571) 272-0674. If Applicants are unable to reach Mukund Shah within 24-hour period, they may contact James O. Wilson, Acting-SPE of art unit 1624 at 571-272-0661.

The fax phone number for the organization where this application or proceeding is assigned (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

*Venkataraman Balasubramanian*  
Venkataraman Balasubramanian

2/21/2005